

Welcome to the Essigmann Lab Home Page



The Essigmann Group

Department of Chemistry
Massachusetts Institute of Technology

Biological Engineering Division

Research Link.

Lab

• Things to do and see on our Web Page

Essigmann Research Group

- Lab Research
- Current Group Members

- Alumni
- About John Essigmann
- How to Reach the Essigmann Lab from the T
- The Essigmann Cabin in Maine
- New photos from Spring 2001
- ET Gets a Job! -- Elizabeth Trimmer started in the fall of 2000 as an Assistant Professor of Chemistry at Grinnell College
- Hyun-Ju gets one too! Assistant Professor of Medicinal Chemistry at Sungkyunkwan University
- Bill Kobertz just started as Assistant Professor of Biochemistry and Pharmacology at the University of Massachusetts Medical School
- Michelle "5-for-5" Hamm started this fall as Assistant Professor of Chemistry at the University of Richmond
- And Kevin Yarema is Assistant Professor of Biomedical Engineering at Johns Hopkins University
- Maryann Smela is Staff Scientist at Momenta Pharmaceuticals
- Beatriz Zayas-Rivera is Assistant Professor at the Universidad Metropolitana in Puerto Rico
- Kaushik Mitra has just taken a job with Merck Pharmaceuticals
- Guess Who Won The MIT \$50K Competition?

John's MIT and Thailand Courses

- MIT Course 5.07 (Biological Chemistry)
- Titanic Picture from 5.07
- MIT Course 5.22J/10.02J/BE105J (Biotechnology and Engineering): Stent Case Study
- MIT Course 5.22J/10.02J/BE105J (Biotechnology and Engineering): Ritalin Case Study
- MIT Course BE214 (Human Pathophysiology)
- Bioengineering and Environmental Health Course Taught in Thailand during the summer of 2002 Tuberculosis Case Study



Other Important Stuff

- Nolan Essigmann's Homepage
- Charles River Gymnastics
- BE Seminar Homepage (2002-2003)
- BE Seminar Homepage (2003-2004).
- MIT Students: If you want a Letter of Recommendation from John Essigmann, kindly follow these instructions
- **Simmons Hall**

c/o

Essigmann Group, ptrye@mit.edu

02/08/2004

		<h1>Paclitaxel (Taxol)</h1> <h2>Mechanism of Action</h2>			
Home		Paclitaxel	Docetaxel	Order	Contact
	Paclitaxel Story	Paclitaxel full information	Paclitaxel Injection full information	Paclitaxel Clinical Trials	Paclitaxel mechanism
	Quality Control of Paclitaxel bulk	Quality Control of Paclitaxel Injection	Paclitaxel Patents	Price	How to Order

Someone said Paclitaxel (Taxol) is a "billion dollar molecule".

The last decade witnessed the introduction of exciting new chemotherapeutic agents. Among these, Paclitaxel emerged as one of the most popular anti-cancer drugs.

Paclitaxel has activity against a broad band of tumour types, including breast, ovarian, lung, head and neck cancers. Paclitaxel also has activity in other malignancies that are refractory to conventional chemotherapy, including previously-treated lymphoma and small cell lung cancers and oesophageal, gastric endometrial, bladder and germ cell tumours. Paclitaxel is also active against AIDS-associated Kaposi's sarcoma.

Here we do a brief discussion about why and how Paclitaxel becomes such an important agent in cancer treatment.

What is a Cancer Cell?

The various organs of the human body are made up of different types of cells. Any cell type can grow into a primary cancer. Cancers from different cell types behave differently. That's why there are so many different types of cancers.

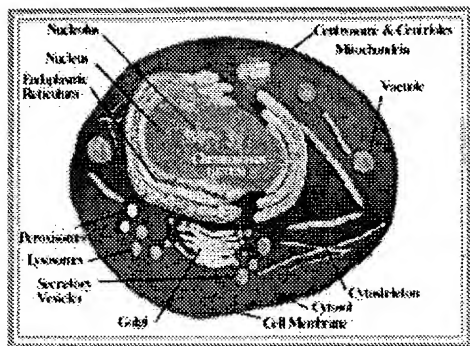
Human cells are pre-programmed to reproduce up to 50 or 60 times maximum. Then they will eventually die. Stem cells provide a pool of dividing cells that the body uses to restock.

What is cancer cell? It is a 'immortal' cell who lost control. It keep on dividing and spreading, it do not obey to the regular rules and it do not die but go on and on reproducing. Eventually a tumour is formed that is made up of billions of copies of the original cancer cell.

Now the major task of all anti-cancer drugs is to stop the cancer cells growing. Scientists have tried to block the cell growth cycle on any point.

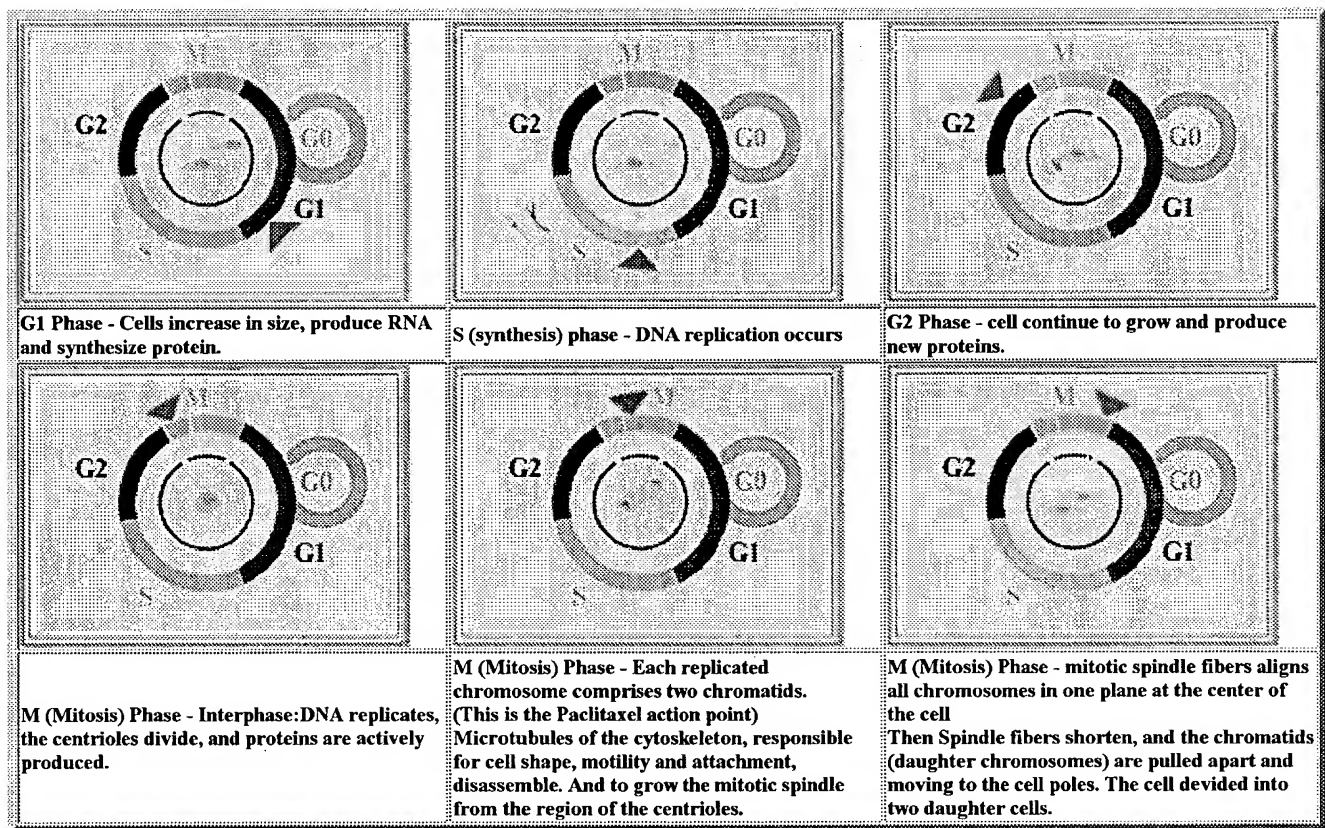
The success of Paclitaxel (Taxol) and Docetaxel (Taxotere) largely due to its unique mechanism of action - It promotes the polymerisation of tubulin, thereby causing cell death by disrupting the normal microtubule dynamics required for cell division and vital interphase processes.

The Structure of A Human Cell:

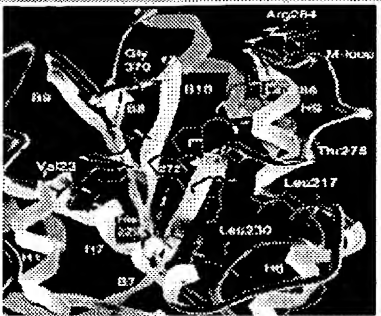
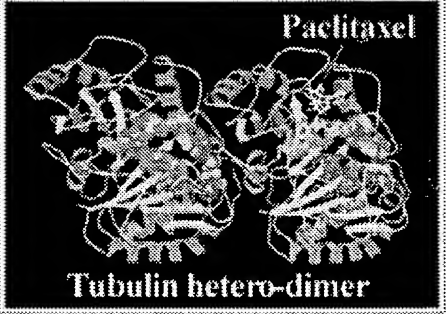
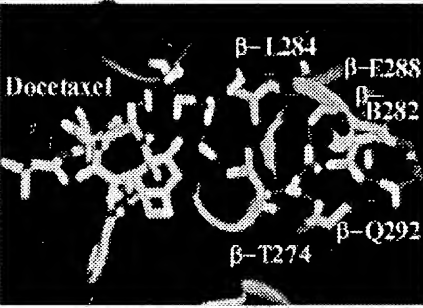


Cell Cycle: How Cells Reproducing?

Cell Growth Cycle including 4 stages: G1Phase - S Phase - G2 Phase - M Phase. (G0 phase occurs in special case when the cell take a sleep - arrest.)



What does Paclitaxel do in the Cell?

	<p>The binding conformation of Paclitaxel in β-tubulin - Scientists using electron crystallography etc technology determined the binding site of Paclitaxel in tubulin.</p> <p>The Paclitaxel molecule shows a T-shaped or butterfly structure is optimized within the beta-tubulin and exhibits functional similarity to a portion of the B9-B10 loop in the alpha-tubulin. This conformation operating as a center of organization for a diversity of secondary structures. It permit intermolecular hydrophobic association as seen for the irregularly stacked C-3' benzamido, His-229, and C-2 benzoyl moieties.</p> <p>It brought the binding affinity, photoaffinity labeling, and acquired mutation in human cancer cells.</p>
<p>Paclitaxel binding to Tubulins hetero-dimer - α- Tubulin and β-Tubulin are the basic units of Microtubule. This 3D model shows the Paclitaxel molecule binding Tubulin and make it staged together. The Microtubules cannot disassemble, the cell cannot dividing.</p>	
	<p>Docetaxel.3H₂O and Tubulin - Docetaxel (orange) is hydrogen bonded to waters (white) that form a contiguously hydrogen-bonded solvent network. The backbone ribbon structure of tubulin. The amino acids illustrated are residues that are principally involved in determining the location of these solvent molecules.</p>

Resistance to Paclitaxel:

Mechanisms of acquired resistance to paclitaxel include

The overexpression of the membrane P-glycoprotein (P-gp) that function as drug-efflux pumps.

Or the alterations of tubulin structure, the alpha- and beta-tubulin isotypes or changes in the drug-binding affinity of the microtubules.

Paclitaxel, Docetaxel and New Drugs in the same Category of mode of action:

The unique cytotoxic mechanism of Paclitaxel - the stabilization of microtubules leading to mitotic

arrest - is now shared by Docetaxel, Eleutherobin, Epothilones A and B, and Discodermolide as well as some new compounds.

There have been clinical trials to compare the efficacy and safety of Paclitaxel and Docetaxel. Some results suggest that Docetaxel may be superior to Paclitaxel in the treatment of certain cancers like metastatic breast cancer.

Currently the high price of Docetaxel make it much less affordable for cancer patients. However when the generic Docetaxel Injection arrives with lower price, its potential applications will be expected.

To improve the performance of Paclitaxel, many delivery system are on developing. The oral Paclitaxel clinical trials are on going.

The synthesis of new taxoids with improved biological activity is still an important research area today.

By 21CEP Research Group - Feb. 2003

Site map:

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